

As displayed in the examples above an effective concentration of a nitric oxide releasing substance selected from a member of the group consisting of L-arginine, L-arginine salts and L-arginine derivatives is (0.25% to 25%), when used in combination of salts each having a concentration of (0.25% to 25%).

*F1 (uncd)*  
In the case of creating a high ionic strength ions such as but not limited to sodium chloride, potassium chloride, choline chloride, magnesium chloride, lithium chloride, alone or in combination were added in high concentration.

---

## REMARKS

### I. CLAIM STATUS

Claims 33-35, 38-44, 47-53, 56-59 and 61-63 stand rejected.

Claims 33-35, 38-44, 47-53, 56-59 and 61-63 remain pending.

### II. SPECIFICATION AMENDMENTS

The applicant respectfully amends the specification to include the contents of originally filed claims 1 and claims which depend upon claim 1 drawn to method of increasing bloodflow and claim 12 and the claims which depend upon claim 12 drawn to a method of treating male sexual dysfunction.

As Examiner is aware that the contents of claims, abstract and any drawings present at the time of filing may be amended into the body of the specification

without creating any new matter issues. (See *Bocciarelli v. Huffman*, 232 F.2d 647, 109 USPQ 385, 388 (C.C.P.A. 1956)) Therefore this amendment of the specification contains **no new matter**.

### III. REJECTION UNDER 35 U.S.C. 112(1)

Claims 33-35, 38-44, 47-53, 56-59 and 61-63 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification . . . to one skilled in the art that the inventor, at the time the application was filed, had possession of the claimed invention. The applicant respectfully disagrees with the Examiner's contention that "applicant's concentration ranges are therefore new matter" statement which is incorrect since **claim amendments** are never considered new matter (See *In re Rasmussen*, 650 F. 2d 1212, 211 USPQ 323, 326 (C.C.P.A. 1981), but may not be support sufficiently by the specification. Applicant responds to the reasonable rejection by Examiner under 112(1) that the amendments lack sufficient support through amending the specification to clearly support the ranges asserted.

The Examiner's argument that the there is "but at most only such concentrations for specific compositions" is both factually and legally incorrect reasoning (See *In re Smythe*, 480 F.2d 1376, 178 USPQ 279, 285 (C.C.P.A. 1973) discussing inherently disclosing) because the specification on page 6

**clearly** indicates that the invention can use various forms of L-arginine and therefore one skilled in the art would be sufficiently taught by this specification to use this range for all forms. Furthermore this range was a dependent claim drawn to the genus of L-arginine and was used in multiple of different species of L-arginine not just one and therefore inherently disclosed that it applied to all unless taught otherwise.

Claims 33-35, 38-44, 47-53, 56-59 and 61-63 are now fully in compliance with the requirements under 35 U.S.C. 112(1) with the proper amendment of the specification and the applicant respectfully requests removal of the rejection.

#### IV. REJECTION UNDER 35 U.S.C. 112(2)

Claims 33-35, 38-44, 47-53, 56-59 and 61-63 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim what the applicant regards as the invention.

Applicant respectfully disagrees with the Examiners mischaracterization of the limitations of the claim and the contents of the declaration. The applicant's statements are not contradictory only the Examiner's interpretation of the claim and the declaration. Specifically in reference to the declaration referring to the Weuffen patent it states that a concentration of 4.9 grams/liter

**in combination** with the disclosed ions is insufficient to produce a hostile biophysical environment to produce an effective treatment.

The ranges of (0.25% to 25%) for L-arginine is limited by the modifier “an effective amount of the substance” and the salts with the concentration of (0.25% to 25%) are associated with the limitation of “sufficient to create a hostile biophysical environment”. The selection of the lowest concentrations of each would fail to be effective as the limitation requires and thus would not be selected. Hetchman as discussed only teaches application to the sphincter to stop spasms and not the skin as in our claim. There are no contradictory statements and thus one skilled in the art would select the proper concentration combinations as directed in the claim limitations that are not taught or disclosed in the prior art. The applicant respectfully requests that the Examiner review all limitations in the claim and remove the rejection.

#### V. REJECTION UNDER 35 U.S.C. 102/103

Claims 33-34, 38, 51-53 and 59 stand rejected under 35 U.S.C. 102 (a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Weuffen et al. (USP 5,629,002). The applicant disagrees with this assertion because the cited art either singly or in combination fails to produce the instant invention. The court has placed the burden of proof to produce a

factual basis for its rejection of an application under sections 102 and 103.

(See *In re Warner*, 379 F.2d 1011, 154 USPQ 173, 178 (C.C.P.A. 1967))

in cell  
of  
gs ( Claims 33-34, 38, 51-53 and 59 contain the limitations “an effective amount” for the L-arginine and “concentration of an ionic salt sufficient to create a hostile biophysical environment” which are not present in the Weuffen art without resorting to hindsight reasoning based on the applicant’s own disclosure.

Claim 33 stands rejected under 35 U.S.C. 102 (a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hetchman (USP 5,595,753). The applicant respectfully disagrees since the art cited fails either singly or in combination to teach the limitations of the instant claim.

Hetchman teaches the application of L-arginine in a saline solution “an enema” to the “sphincter and smooth muscle spasm in the gastrointestinal tract” (See title and specification) to reduce pain from spasms and hemorrhoids. The cited art does not teach the application of L-arginine to the skin and teach or contain the limitations “an effective amount” for the L-arginine and “concentration of an ionic salt sufficient to create a hostile biophysical environment” which are not present in the Hetchman art without resorting to hindsight reasoning based on the applicant’s own disclosure.

Claims 61-63 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Garfield et al. in view of Hechtman, Altodonna (USP

5,853,768) Cooke et al. (USP 5,428,070), Saavedra et al. (5632,981) and Cooper et al. The applicant disagrees with the Examiner's rejection because it fails to teach each and every limitation of the instant claims. Garfield teaches specific direct nitric oxide donors have beneficial effects. See Column 2, lines 53-56 teaching "Present NO Donors: Presently there are only a few nitric oxide donor compounds that are used clinically....Table 1 indicates various NO donors agents with clinical potential". Table 1 (not presented herein) does not disclose L-arginine and the specification background discusses that L-arginines beneficial use is for internal consumption because of enzymatic breakdown requirements. Hetchman as discussed is applied internally to the interior of the anus to the sphincter to reduce pain or spasming. The anus is a different structure and mechanism of trasfer than that of the skin (outer epidermal layer) and therefore it does not teach the application to the skin as the instant claims of the application. Altodonna is silent to the presence of the application of L-arginine to the skin for any purpose and its combination would not motivate to take L-arginine from their anus and rub it on their skin. Cooke teaches the application of L-arginine internally only.

The art cited in combination therefore is completely silent regarding the teaching of the application of L-arginine to the skin in the claimed delivery vehicle. Without using the teachings provided from the applicants own disclosure the Examiner fails to provide a prima facia case of obviousness.

Therefore the applicant respectfully requests reconsideration and allowance of the claims.

MARKED UP SPECIFICATION

A method of delivering a nitric oxide releasing substance selected from a member of the group consisting of L-arginine, L-arginine salts and L-arginine derivatives, to skin comprising the step of topically applying to the skin a delivery vehicle for the substance, said delivery vehicle containing an effective amount of the substance, and a concentration of ionic salt sufficient to create a hostile biophysical environment which causes the substance to migrate from the delivery vehicle to the skin where the substance is absorbed by tissue wherein [a] said delivery vehicle comprises water (20-80%), mineral oil (3-18%), glyceryl stearate (0.5-12%), squalene (0.2-12%), cetyl alcohol (0.1-11%), propylene glycol stearate (0.1-11%), wheat germ oil (0.1-6%), glyceryl stearate (0.1-6%), isopropyl myristate (0.1-6%), stearyl stearate (0.1-6%), polysorbate 60 (0.1-5%), propylene glycol (0.05- 5%), tocopherol acetate (0.5-5%), collagen (0.05-5%), sorbitan stearate (0.05-5%), vitamin A&D (0.02%-4%), triethanolamine (0.01-4%), methylparaben (0.01-4%), aloe vera extract (0.01-4%), imidazolidinyl urea (0.01-4%), propylparaben (0.01-4%), bha (0.01-4%), L-arginine hydrochloride (0.25% to 25%), sodium chloride (0.025% to 25%), and magnesium chloride (0.25% to 25%) is applied to the skin.

A method of treating impotence in a male comprising delivering a nitric oxide releasing substance selected from a member of the group consisting of L-arginine, L-arginine salts and L-arginine derivatives, to skin comprising the step of topically applying to the penis a delivery vehicle for the substance, said delivery vehicle containing an effective amount of substance, and a concentration of ionic salt sufficient to create a hostile biophysical environment which causes the substance to migrate from the vehicle to the penis where the substance is absorbed by tissue wherein [a] said delivery vehicle comprises water (20-80%), mineral oil (3-18%), glyceryl stearate (0.5-12%), squalene (0.2-12%), cetyl alcohol (0.1-11%), propylene glycol stearate (0.1-11%), wheat germ oil (0.1-6%), glyceryl stearate (0.1-6%), isopropyl myristate (0.1-6%), stearyl stearate (0.1-6%), polysorbate 60 (0.1-5%), propylene glycol (0.05- 5%), tocopherol acetate (0.5-5%), collagen (0.05-5%), sorbitan stearate (0.05-5%), vitamin A&D (0.02%-4%), triethanolamine (0.01-4%), methylparaben (0.01-4%), aloe vera extract (0.01-4%), imidazolidinyl urea (0.01-4%), propylparaben (0.01-4%), bha (0.01-4%), L-arginine hydrochloride (0.25% to 25%), sodium chloride (0.025% to 25%), and magnesium chloride (0.25% to 25%) is applied to the penis.

As displayed in the examples above an effective concentration of a nitric oxide releasing substance selected from a member of the group consisting of L-arginine, L-arginine salts and L-arginine derivatives is (0.25% to 25%), when



used in combination of salts each having a concentration of (0.25% to 25%).

In the case of creating a high ionic strength ions such as but not limited to sodium chloride, potassium chloride, choline chloride, magnesium chloride, lithium chloride, alone or in combination were added in high concentration.

### CONCLUSION

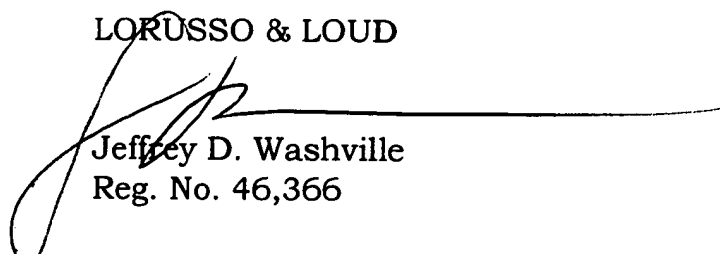
The applicant respectfully requests allowance of all claims, because the claims are not taught by the cited art either singly or in combination. Fee free to call collect with any questions regarding this submission

Dated July 22, 2002

Respectfully submitted,

LORUSSO & LOUD  
440 Commercial Street  
Boston, MA 02109  
Phone: (617) 227-0070  
Fax: (617) 723-4609

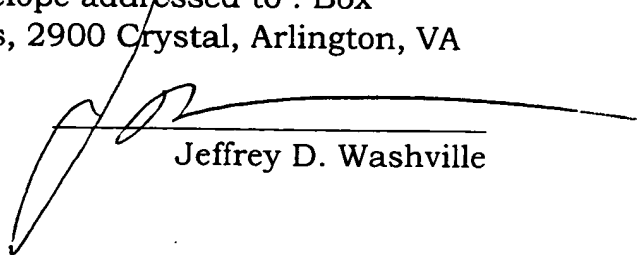
LORUSSO & LOUD



Jeffrey D. Washville  
Reg. No. 46,366

### **Certification Under 37 CFR § 1.8**

I hereby certify that this Response is being deposited with the United States Postal Service on 22 JUL 2002, in an envelope addressed to : Box Amendment, Assistant Commissioner for Patents, 2900 Crystal, Arlington, VA 22202.



Jeffrey D. Washville